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Request for grant of a patent

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16 DEC 2002

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1. Your reference 8627 GB CAH/EAD

2. Patent application number *(The Patent Office will fill in this part)* 0229263.9

3. Full name, address and postcode of the or of each applicant *(underline all surnames)*

DIAMETRICS MEDICAL LIMITED
Short Street
High Wycombe
Buckinghamshire
England
HP11 2QH

Patents ADP number *(if you know it)* 7193345001

If the applicant is a corporate body, give the country/state of its incorporation UK

4. Title of the invention Improvements in or relating to sensor devices for monitoring the condition of a human or animal patient

5. Name of your agent *(if you have one)* Abel & Imray

"Address for service" in the United Kingdom to which all correspondence should be sent *(including the postcode)*

20 Red Lion Street
London
WC1R 4PQ
United Kingdom

Patents ADP number *(if you know it)* 174001

6. If you are declaring priority from one or more earlier patent applications, give the country and the date of filing of the or of each of these earlier applications and *(if you know it)* the or each application number

Country	Priority application number *(if you know it)*	Date of filing *(day / month / year)*

7. If this application is divided or otherwise derived from an earlier UK application, give the number and the filing date of the earlier application

Number of earlier application	Date of filing *(day / month / year)*

8. Is a statement of inventorship and of right to grant of a patent required in support of this request? *(Answer 'Yes' if:*

a) any applicant named in part 3 is not an inventor, or
b) there is an inventor who is not named as an applicant, or
c) any named applicant is a corporate body.
See note (d))

Yes

[redacted] Form 1/77

9. Enter the number of sheets for any of the following items you are filing with this form. Do not count copies of the same document

Continuation sheets of this form	
Description	13
Claim(s)	5
Abstract	
Drawing(s)	1

10. If you are also filing any of the following, state how many against each item.

Priority documents	
Translations of priority documents	
Statement of inventorship and right to grant of a patent *(Patents Form 7/77)*	
Request for preliminary examination and search *(Patents Form 9/77)*	1
Request for substantive examination *(Patents Form 10/77)*	
Any other documents *(please specify)*	

11. I/We request the grant of a patent on the basis of this application.

Signature Abel & Imray Date 16/12/02

12. Name and daytime telephone number of person to contact in the United Kingdom: Ceris Humphreys - 020 7242 9984

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Fig.1.

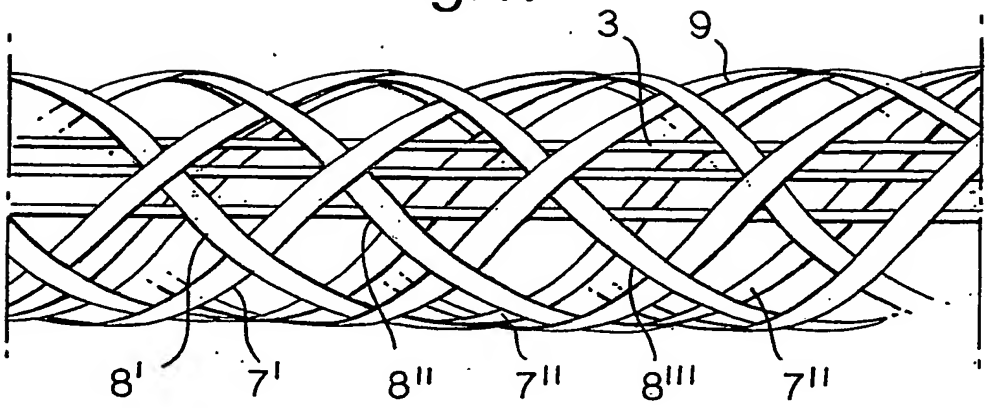


Fig.2.

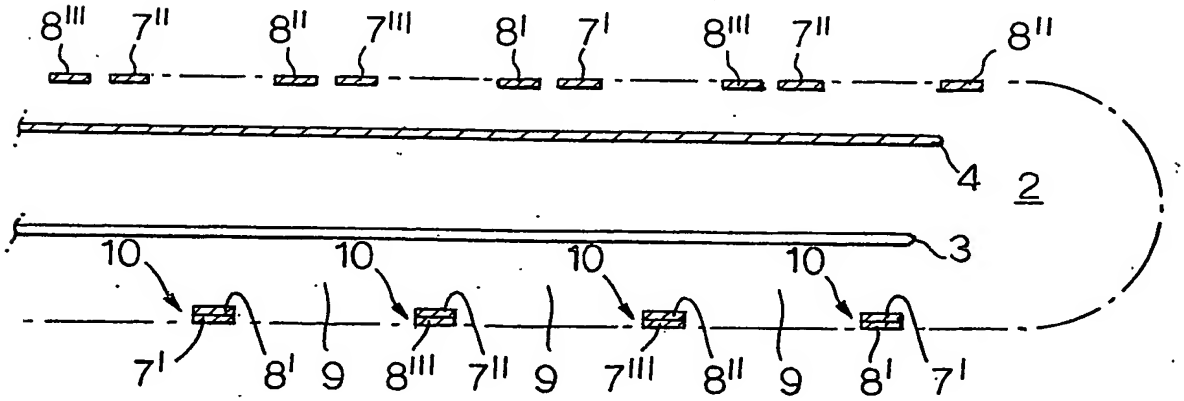
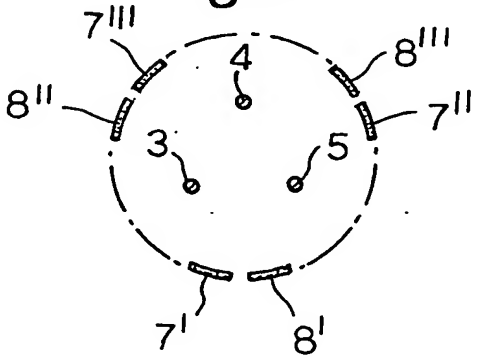


Fig.3.



Improvements in or relating to sensor devices for monitoring the condition of a human or animal patient

The invention relates to sensor devices for clinical use and in particular to sensor devices for monitoring the concentration of one or more analytes in human or animal patients.

The measurement in blood or other bodily fluids of certain analytes, for example, dissolved oxygen, carbon dioxide and hydrogen (which may be expressed as partial pressure of oxygen and carbon dioxide, (referred to hereafter as pO_2 and pCO_2 respectively and as pH), can be important during surgery, post-operatively and during hospitalisation under intensive care. In certain known forms of sensor device, a probe can be placed in the patient, for example in a blood vessel, in other bodily fluid or in tissue. The probe may contain indicators, for example absorption and fluorescent indicators, which are arranged to provide data regarding certain analytes in the fluid or tissue, and to transmit that data to a base unit which in use of the sensor device is located outside the patient's body. One such sensor device, based on optical detection means, is known as the Paratrend Continuous Blood Gas Monitor available from Diametrics Medical Limited of High Wycombe, England, and can measure pO_2, pCO_2 and pH. Analyte concentrations *in vivo*

can also be determined non-optically, for example, using electro-chemical sensors.

In certain circumstances, and in particular where fine and/or delicate probes are used in tissue or in cerebrospinal fluid, the probes may be exposed to unacceptable stresses, resulting in kinking, compression or breakage of the probe. Those stresses may arise on insertion of the probes, for example into muscle or other dense tissue, on usage, for example as a result of patient movement or muscle contraction at the site of use, or on withdrawal of the probe after use.

Accordingly, there is a need for sensor devices which have sufficient strength to withstand more effectively the stresses to which they will be subjected in use.

The invention provides a sensor device for use in a human or animal, comprising a probe within which there is located a sensor for an analyte, the sensor device comprising a mesh structure enveloping at least a portion of said probe.

The mesh structure is able to provide strength to the sensor structure whilst nonetheless offering good flexibility characteristics and permitting access of analytes to the probe and to the sensor or sensors therein. It is believed that the strength of the mesh-enveloped sensor device arises at least in part from the way in which

a mesh structure spreads a locally applied load. Furthermore, the mesh structure can eliminate the possibility of breakage of the sensor device on retraction.

Many mesh structures are, as a consequence of their structure, expansible. That can offer particular advantages in manufacture of the sensor devices in that the mesh structure can allow for a void of relatively large diameter to be adopted for insertion of parts during construction of the sensor whilst permitting a smaller diameter to be adopted thereafter in which the strengthening characteristics of the mesh structure are optimally utilised.

The mesh structure advantageously comprises a plurality of filaments, and preferably a multiplicity of filaments. The term "filaments" is used herein to refer to any elongate strand irrespective of its cross-sectional configuration and structure, and includes for example strands of flat cross-sectional configuration which might be referred to as "strips" or "ribbons". Advantageously, the filaments are strips of elongate cross-section. Advantageously, the strips have a depth of not more than 100 μm, for example, from 5 to 100 μm, and preferably from 10 to 15 μm. Advantageously, the strips have a width of not more than 50 μm. Advantageously, the strips are of width from 5 μm to

50 μm.

Advantageously, the mesh structure comprises a plurality of helically wound filaments, at least a first said filament extending helically in the opposite sense to at least a second said filament. Preferably, the mesh structure comprises a first group of filaments, for example strips, extending in a first helical sense, and a second group of filaments, for example strips, extending in a second helical sense, opposed to the first. The pitch between adjacent windings of each filament or, where there is a group of filaments, between adjacent filaments is so chosen that the open area not occupied by filaments is approximately from 0.3 to 0.7 cm^2 per cm^2 of the mesh structure, for example, about 0.5 cm^2 per cm^2 of the mesh structure in at least a region of the mesh structure in the vicinity of a sensor within the device. Preferably, the helical filament(s) extending in a first helical direction is/are interwoven with the helical filament(s) extending in a helical direction opposed to the first.

Preferably, the mesh structure comprises a multiplicity of interwoven filaments. In another form of device, the mesh structure comprises a knitted mesh.

In some circumstances, first and second filaments may be joined to one another at points of overlap therebetween. Advantageously, points of overlap between filaments are welded. Although attachment of the filaments at points of overlap may reduce the flexibility of the sensor device, it may improve the dimensional stability of the mesh structure and thus of the sensor device, providing increased strength in use.

Advantageously, the mesh structure comprises filaments comprising a metallic material. For example, the filaments may comprise metallic ribbon. Advantageously, the filaments comprise at least one metal selected from the group consisting of stainless steel, titanium and gold. Preferably, the filaments comprise a metallic core coated by a plastics material.

The mesh structure may comprise filaments of plastics material, for example, a synthetic polymer material selected from the group consisting of polyamides, polyesters, polyurethanes, polyolefins and fluoropolymers, for example, polytetrafluoroethylene (PTFE).

Advantageously, points of contact between filaments are welded.

Advantageously, the mesh structure is constructed from

monofilaments. If desired, the mesh structure can be constructed of multifilament yarns. Preferably, the mesh structure is a braid.

Advantageously, the mesh structure defines an open area between adjacent filaments which constitutes at least 30% of the total surface area of the mesh (including the openings). It is a simple matter for the skilled person to select an appropriate weave pattern and density for achieving a desired magnitude of open area, and taking account of the width of the filaments to be used.

Preferably, the permeable material of the matrix extends at least partially into the openings. More preferably, the permeable material substantially fills the opening, whereby the mesh structure and the permeable material filling said openings define a substantially smooth outer surface of the sensor device.

Preferably, the mesh structure is a mesh sleeve. Advantageously, the external diameter of the mesh sleeve is from 0.5 to 1mm.

Preferably, the mesh structure has a resistance to kinking and breakage which is such that the sensor device will not normally be subject to kinking or breakage when inserted into myocardial tissue and subjected to normal contractions thereof.

Advantageously, the mesh structure comprises first and second analyte sensors embedded in the matrix, the matrix being permeable to at least first and second analytes to be determined respectively by said first and second sensors. Advantageously, the sensor device comprises a sensor for determining at least one parameter selected from pO_2, pCO_2 and pH. Preferably, the device comprises a first sensor for pO_2, a second sensor for pCO_2 and a third sensor for pH. Advantageously, the sensors are optical sensors. Advantageously, the device further comprises a temperature measurement device, for example, a thermocouple.

The sensor device may be used in blood vessels for monitoring blood analytes or may be used in tissue, for example in muscular tissue or in organs. The strength of the device makes it suitable for use even in muscles which can be subjected to strong contractions, including the myocardium, or in bodily fluids or tissues to which access can be obtained only through relatively dense tissue, for example, where the device is required to be sited in cerebrospinal fluid.

As already mentioned, it is preferable for the mesh structure to be in the form of a sleeve. Preferably, the diameter of the sleeve may be reduced by applying tension to the sleeve in the axial direction. Such structures offer

particular advantages in manufacture of the sensor device in that the sensors, which may comprise one or more analyte sensors and one or more sensors for physical parameters, for example, temperature, may be inserted through a proximal end of the tube whilst the tube diameter is relatively large, and tension may subsequently be applied axially to the tube so as to collapse it around the bundle of sensors. The distal end of the mesh structure may then be closed, for example, with a polyethylene plug which may be heated to permit joining thereof to the mesh structure. The void spaces within the mesh structure, including between the filaments of the mesh structure itself may then be filled by a filling material that is permeable to the analyte(s) to be determined, for example, by a hydrophilic gel. As hydrophilic gel there may be used any suitable hydrophilic gel that will permit the transport of hydrogen ions and the dissolved gases to be detected. Suitable hydrogels include, for example, carboxymethylcellulose gels and, especially, polyacrylamide gels. The use of hydrogels, in particular, polyacrylamide gels, as a matrix in blood gas sensors is known and the gels can be incorporated in the sensor devices of the present invention by means analogous to those known and used for the manufacture of the known sensor devices.

Advantageously, the mesh sleeve is arranged to have an external diameter of 0.5 to 1 mm in the sensor device, and to have an expanded external diameter of exceeding 1 mm, for example, of at least 1.5 mm.

Thus, the invention also provides a method of making a sensor device, comprising maintaining a mesh sleeve in a first, expanded, configuration, inserting one or more sensors into the mesh sleeve in said expanded configuration, causing the mesh sleeve to adopt a second, contracted configuration in which it has a smaller internal diameter than in the first configuration, and closing at least a distal end of the mesh sleeve to enclose the sensor(s). Preferably, the mesh structure and enclosed sensor(s) are subjected to a treatment in which a gel is formed in void regions, inside the mesh sleeve and in open regions of the sleeve itself.

The invention further provides a method of monitoring myocardial tissue, comprising inserting into the myocardium of a patient a flexible sensor probe comprising a housing and a sensor therein for at least one analyte and monitoring the at least one analyte. Advantageously, at least one analyte comprises one or more blood gases. The concentration of blood gases and especially oxygen in myocardial tissue provides valuable information regarding

the efficiency of myocardial perfusion and may be particularly advantageous during cardiac or coronary surgery and post-operatively when it can give early warning of the failure of perfusion or of the failure successfully to reperfuse following surgery.

The use of rigid sensors in the myocardium is known in, for example, the Khuri myocardial pH monitoring system made by Terum. Cardiovascular Systems Corporation of Tustin California and in a device described in Clinical Science (2000) 98, 321-328 ("Myocardial tissue oxygen supply and utilisation during coronary artery bypass surgery: evidence of microvascular no-reflow"). In contrast to the rigid structures described in those prior disclosures, however, the method of the present invention in which a flexible sensor probe is used provides for greater selectivity in the siting of the sensor probe within the myocardium, in some cases possibly also reducing the disruption and/or damage to immediately surrounding tissue. In the method of the invention any suitable form of sensor(s) may be used. Advantageously, however, there is present in the probe one or more analyte sensors which are optical sensors.

Certain illustrative embodiments of the invention will now be described in detail with reference to the accompanying drawings, in which:

Fig. 1 is a perspective view of a probe of a sensor device according to the invention;

Fig. 2 is a longitudinal section through an end portion of the probe; and

Fig. 3 is a transverse section through an end portion of the probe.

With reference to Fig. 1, a sensor device 1 has a probe which is suitable for insertion into a blood vessel or into tissue. The probe has a matrix 2 of a hydrophilic gel, for example, a polyacrylamide gel. Embedded in the matrix 2 are a first optical sensor 3 for determining oxygen partial pressure (pO_2), a second sensor 4 for determining carbon dioxide partial pressure (pCO_2), and a third sensor 5 for determining pH. The matrix 2 is permeable to hydrogen ions and to oxygen and carbon dioxide. The matrix 2 is partially enveloped by mesh structure 6, which is made up of two groups 7, 8 of helically wound metal ribbons. A first group 7 of said helically extending metal ribbons has three equally spaced ribbons 7^{1}, 7^{11} and 7^{111}. The second group 8 of ribbons has three equally spaced ribbons 8^{1}, 8^{11} and 8^{111}. Each ribbon 7^{1}, 7^{11} and 7^{111} alternately overlies and underlies the ribbons of group 8 at points of overlap so as to form an essentially woven sleeve. The groups 7, 8 of filaments define a mesh structure having openings 9, each of

which has a diameter of about 0.7mm. (The diameter in relation to the openings, when not circular, is to be taken to be the largest distance between two separate points on the perimeter of the opening).

The openings 9 are filled with hydrophilic gel, which is integral with the rest of the matrix 2.

Referring to Fig. 2, the ribbons of group 7 overlie or underlie the ribbons of group 8 at points of overlap 10. The ribbons may, if desired, be welded together at the points 10, but are not welded in the embodiment shown.

Fig. 3 is a transverse section through the embodiment of Figs. 1 and 2.

The probe can be inserted into a blood vessel in known manner through a catheter. It can also be inserted into soft tissue, for example, into muscular tissue or an organ. It may be introduced using a needle, for example, of the kind disclosed in WO 01/78588. The mesh imparts strength to the sensor device, and enhances resistance to kinking. It can also prevent disintegration of the probe when the probe is retracted from the patient, and provides support to the sensor device on insertion. Moreover, when the sensor device is used in regions in which it will be subjected to significant stresses, the mesh structure can prevent kinking and breakage. By way of example, the mesh structure may

prevent damage resulting from movement of the patient. It is in particular envisaged that the sensor device of the invention will offer advantages when used to monitor myocardial function, where the probe may be subjected to severe stresses as a result of the strong systolic contraction of the myocardium.

Claims

1. A sensor device for use in a human or animal, comprising a probe within which there is located a sensor for an analyte, the sensor device comprising a mesh structure enveloping at least a portion of said probe.

2. A sensor device according to claim 1, in which the mesh structure comprises a plurality of filaments.

3. A sensor device according to claim 2, in which the mesh structure comprises a multiplicity of filaments.

4. A sensor device according to any one of the preceding claims, in which the filaments are strips of elongate cross-section.

5. A sensor device according to claim 4, in which the strips are of width from 5 μm to 50 μm.

6. A sensor device according to claim 4, in which the strips are of depth from 5 μm to 50 μm.

7. A sensor device according to any one of the preceding claims in which the mesh structure defines an open area of at least 0.3 cm^2 per cm^2 of the mesh structure.

8. A sensor device according to any one of the preceding claims, in which the mesh structure defines an open area of not more than 0.7 cm^2 per cm^2 of the mesh structure.

9. A sensor device according to any one of the preceding claims, in which the mesh structure comprises a plurality of

helically wound filaments, at least a first said filament extending helically in the opposite sense to at least a second said filament.

10. A sensor device according to any one of the preceding claims, in which the mesh structure is a woven mesh structure.

11. A sensor device according to any one of the preceding claims, in which the mesh structure comprises a multiplicity of interwoven filaments.

12. A sensor device according to any one of the preceding claims, in which first and second filaments are joined to one another at points of overlap therebetween.

13. A sensor device according to any one of the preceding claims, in which the mesh structure comprises filaments comprising a metallic material.

14. A sensor device according to claim 13, in which the filaments comprise metallic ribbon.

15. A sensor device according to claim 13 or claim 14, in which the filaments comprise at least one metal selected from the group consisting of stainless steel, titanium and gold.

16. A sensor device according to any one of claims 13 to 15, in which the filaments comprise a metallic core coated by a plastics material.

17. A sensor device according to any one of the preceding claims, in which the mesh structure comprises filaments of plastics material.

18. A sensor device according to claim 14, in which the filaments comprise a synthetic polymer material selected from the group consisting of polyamides, polyesters, polyurethanes, polyolefins and fluoropolymers.

19. A sensor device according to any one of the preceding claims in which points of overlap between filaments are welded.

20. A sensor device according to any one of the preceding claims, in which the mesh structure is constructed from monofilaments.

21. A sensor device according to any one of claims 1 to 19, in which the mesh structure is constructed of multifilament yarns.

22. A sensor device according to any one of the preceding claims, in which the mesh structure is a braid.

23. A sensor device according to any one of the preceding claims, in which the probe comprises a matrix of a permeable material, and the sensor is located within the matrix.

24. A sensor device according to claim 23, in which the mesh defines openings, and the permeable material of the matrix extends at least partially into the openings.

25. A sensor device according to claim 24, in which the permeable material substantially fills the opening, whereby the mesh structure and the permeable material filling said openings form a substantially smooth outer surface of the sensor device.

26. A sensor device according to any one of the preceding claims, in which the mesh structure is a mesh sleeve.

27. A sensor device according to claim 26, in which the external diameter of the mesh sleeve is from 0.5 to 1mm.

28. A sensor device according to any one of the preceding claims, in which the probe comprises first and second analyte sensors embedded in a matrix, the matrix being permeable to at least first and second analytes to be determined respectively by said first and second sensors.

29. A sensor device according to any one of the preceding claims, comprising a sensor for determining at least one parameter selected from pO_2, pCO_2 and pH.

30. A sensor device according to claim 30, comprising a first sensor for p_{O2}, a second sensor for pCO_2 and a third sensor for pH.

31. A sensor device according to any one of the preceding claims, which further comprises a temperature measurement device.

32. A sensor device substantially as described herein with reference to and as illustrated by any one of Figs. 1 to 3.

33. A method of making a sensor device comprising maintaining a mesh sleeve in a first, expanded, configuration, inserting one or more sensors into the mesh sleeve in said expanded configuration, causing the mesh sleeve to adapt a second, contracted configuration in which it has a smaller internal diameter than in the first configuration, and closing at least a distal end of the mesh sleeve to enclose the sensor(s).

34. A method of monitoring myocardial tissue, comprising inserting into the myocardium of a patient a flexible sensor probe comprising a housing and a sensor therein for at least one analyte.

35. A method according to claim 34, in which the sensor probe comprises one or more optical sensors.

36. A method according to claim 34, in which the sensor probe is inserted before or during cardiac or coronary surgery to monitor blood gas perfusion during surgery.

37. A method according to claim 34, in which the sensor is inserted before, during or after cardiac or coronary surgery to monitor myocardial reperfusion post-operatively.